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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/187,693	11/05/1998	AYA JAKOBOVITS	CELL 4.20 CIP2 CPA	3392

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/187,693	JAKOBOVITS ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/8/04 has been entered.

2. Claims 1-7 are pending and are being acted upon in this Office Action.

3. The disclosure is objected to because of the following informalities: (1) "(SEQ ID NO: 29)" in Brief Description of the Drawing Figures on page 8, Figure 1 does not match with SEQ ID NO: 23 shown in Figure 1. (2) "(SEQ ID NO: 40)" in Brief Description of the Drawing Figures on page 9, Figure 3 does not match with SEQ ID NO: 24 shown in Figure 3. (3) "(SEQ ID NO: 41)" in Brief Description of the Drawing Figures on page 9, Figure 5 does not match with SEQ ID NO: 25 shown in Figure 5. (4) "(SEQ ID NO: 42)" in Brief Description of the Drawing Figures on page 9, Figure 7 does not match with SEQ ID NO: 26 shown in Figure 7. (5) Likewise, The SEQ ID NO in the brief description of drawing for Figures 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, with the SEQ ID NO: shown in the actual Figures 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31, respectively. (6) Symbols on page 16, lines 24, 27 and 31 appear to be misplaced. (7) SEQ NO in Brief Description of the Drawing Figures on page 19 for Figure 71 does not match with the SEQ ID NO: in the actual Figure 71. (8) "Figure 82" on page 21 line 10 should have been Figure 82 A-C. (9) "Figure 83" on page 21 line 12 should have been Figure 83 A-B. (10) "Figure 85" on page 21 line 16 should have been Figure 85 A-D. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/40210 (Dec 1996; PTO 1449).

The WO 96/40210 publication teaches various human EGF receptor antibody that binds to human EGF receptor expressing on A431 epidermal carcinoma cells (See entire document, page 22, lines 25-26, pages 41-53, in particular). The reference human antibody inhibits EGF-induced phosphorylation of the EGFR (See page 7, lines, 3-7, Figure 8, in particular). The reference human antibody is less immunogenic than antibody from mouse (See page 3, lines 5-20, in particular). While the reference is silent that the reference antibody has the functional properties of inhibiting the degradation of EGF-r, inhibiting the EGF induced degradation of EGF-r, protects threonine phosphorylation of EGF-r, protects threonine phosphorylation of a 63 KD protein, inhbiting VEGF production by tumor cells by greater than 50% and inhibiting VEGF production by endothelial cells by greater than 40% wherein the tumor cells are A431 or ECV304 cells, the reference antibody has the specificity of the claimed antibody and the functional properties would be an inherent property of said antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

6. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/34096 (Oct 1996; PTO 1449).

The WO 96/34096 publication teaches a method of producing human antibody to any antigen such as human EGFR (See entire document, page 13, lines 33-35, page 14, line 25, claim 18 of WO 96/34096 publication, in particular). The WO 96/34096 publication teaches the advantage of the reference antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular). While the reference is silent that the reference antibody has the functional properties of inhibiting the degradation of EGF-r, inhibiting the EGF induced degradation of EGF-r, protects threonine phosphorylation of EGF-r, protects threonine phosphorylation of a 63 KD protein, inhbiting VEGF production by tumor cells by greater than 50% and inhibiting VEGF production by endothelial cells by greater than 40% wherein the tumor cells are A431 or ECV304 cells, the reference antibody has the specificity of the claimed

antibody and the functional properties would be an inherent property of said antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reins *et al* (of record, J. Cellular Biochemistry 51: 236-248; 1993, PTO 892) in view of WO 96/34096 (Oct 1996; PTO 892).

Reins *et al* teach an antibody such as mab 5-D43 that binds to epidermal growth factor receptor, inhibits tyrosine phosphorylation of EGF receptor (EGF-r) and is readily internalized upon binding to EGFR (See page 239, column 2, Results, page 240, column 2, Fig 1, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the antibody is a human antibody that binds to human epidermal growth factor receptor

The WO 96/34096 publication teaches a method of producing human antibody to any antigen such as human EGFR (See entire document, page 13, lines 33-35, page 14, line 25, claim

18 of WO 96/34096 publication, in particular). The WO 96/34096 publication teaches the advantage of the reference antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the immunogen taught by Reins *et al* for the human EGFR as taught by the WO 96/34096 publication to produce human antibody that binds to human EGFR with the functional properties such as inhibits tyrosine phosphorylation of EGF receptor (EGF-r) and is readily internalized upon binding to EGFR as taught by Reins *et al* and WO 96/34096 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the WO 96/34096 publication teaches the advantage of the human antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular). While the reference is silent that the reference antibody has the property of that recited in claims 1 and 3-7, the molecular weight of this phosphorylated protein to which the reference antibody phosphorylated and the functional properties are the inherent property of the reference antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

10. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Defize *et al* (J Cell Biology 109(5): 2495-507; Nov 1989, PTO 892) in view of WO 96/34096 (Oct 1996; PTO 892).

Defize *et al* teach an antibody that binds to epidermal growth factor receptor such as mAb 2E9 that protects threonine phosphorylation of the EGF receptor (See page 2499, Fig 3C, Table 1, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the antibody is a human antibody that binds to human epidermal growth factor receptor

The WO 96/34096 publication teaches a method of producing human antibody to any antigen such as human EGFR (See entire document, page 13, lines 33-35, page 14, line 25, claim 18 of WO 96/34096 publication, in particular). The WO 96/34096 publication teaches the

advantage of the reference antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the immunogen as taught by Defize for the human EGFR immunogen as taught by the WO 96/34096 publication to produce human antibody that binds to human EGFR with the functional properties such as protects threonine phosphorylation of the EGF receptor as taught by Defoze *et al* and WO 96/34096 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the WO 96/34096 publication teaches the advantage of the human antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular). While the reference is silent that the reference antibody has the property of that recited in claims 1 and 3-7, the molecular weight of this phosphorylated protein to which the reference antibody phosphorylated and the functional properties are the inherent property of the reference antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

11. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petit *et al* (Am J Pathol 15(6):1523-30; Dec 1997, PTO 892) in view of WO 96/34096 (Oct 1996; PTO 892).

Petit *et al* teach an antibody such as C225 that binds to the epidermal growth factor receptor and inhibits VEGF production in A431 cells. The decrease in VEGF production leads to a significantly reduction in tumor blood vessel counts as a consequence of reduction in endothelial cell proliferation (angiogenesis) (See abstract, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the antibody is a human antibody that binds to human epidermal growth factor receptor

The WO 96/34096 publication teaches a method of producing human antibody to any antigen such as human EGFR (See entire document, page 13, lines 33-35, page 14, line 25, claim 18 of WO 96/34096 publication, in particular). The WO 96/34096 publication teaches the

advantage of the reference antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the immunogen as taught by Petit for the immunogen such as human EGFR as taught by the WO 96/34096 publication to produce human antibody that binds to human EGFR with the functional properties such as decreasing in VEGF production that lead to a significantly reduction in tumor blood vessel counts as a consequence of reduction in endothelial cell proliferation (angiogenesis) as taught by Petit *et al* and WO 96/34096 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the WO 96/34096 publication teaches the advantage of the human antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular). While the reference is silent that the reference antibody has the property of that recited in claims 1 and 3-7, the molecular weight of this phosphorylated protein to which the reference antibody phosphorylated and the functional properties are the inherent property of the reference antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

12. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 4,943,533, PTO 892) in view of WO 96/34096 (Oct 1996; PTO 892).

The '533 patent teaches antibodies such as 579, 455, 225, 528, 579 and 455 that bind to epidermal growth factor receptor (See column 3-10 and claims of '533, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the antibody is a human antibody that binds to human epidermal growth factor receptor

The WO 96/34096 publication teaches a method of producing human antibody to any antigen such as human EGFR (See entire document, page 13, lines 33-35, page 14, line 25, claim 18 of WO 96/34096 publication, in particular). The WO 96/34096 publication teaches the advantage of the reference antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the immunogen EGFR as taught by the '533 patent for the human EGFR as taught by the WO 96/34096 publication to produce human antibody that binds to epidermal growth factor receptors from the human epidermoid carcinoma cell line, A-431 and inhibit the growth of said cell line as taught by the '533 patent and WO 96/34096 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the WO 96/34096 publication teaches the advantage of the human antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular). While the reference is silent that the reference antibody has the property of that recited in claims 1 and 3-7, the molecular weight of this phosphorylated protein to which the reference antibody phosphorylated and the functional properties are the inherent property of the reference antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

15. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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